

WHAT IS CLAIMED IS:

1. A method of detecting a polymorphism site,  
comprising:

5 (1) reacting a test sample containing a  
polymorphism site with a plurality of types of probes  
corresponding to a plurality of types of the  
polymorphism site to be identified of said test sample,  
said probes binding to said plurality of types of the  
polymorphism site with a high affinity and being  
10 labeled with marker substances so as to optically  
distinguish from each other; and

(2) optically measuring and analyzing a  
positional change of the marker substance at a  
plurality of time points in the course of the reaction,  
15 thereby detecting the types of polymorphism sites of  
said test sample.

2. The method of detecting a polymorphism site  
according to claim 1, wherein said marker substance is  
a fluorescent substance, said detecting is performed by  
20 a confocal microscope, and said analyzing is performed  
by a fluorescent correlation spectroscopy.

3. The method of detecting a polymorphism site  
according to claim 1, wherein the polymorphism site is  
a single nucleotide polymorphism.

25 4. A method of detecting a polymorphism site,  
comprising:

(1) hybridizing a test sample DNA fragment

containing a sequence of a polymorphism site with  
a plurality of types of DNA probes respectively having  
sequences complementary to a plurality of sequences to  
be identified and contained in the test sample DNA

5 fragment, and labeled with a marker substance, said  
plurality of types of probes being set so as to  
optically distinguish from each other; and

(2) optically measuring and analyzing a change of  
the marker substance at a plurality of time points in  
10 the course of the hybridization, thereby detecting the  
polymorphism site.

5. The method of detecting a polymorphism site  
according to claim 4, wherein said marker substance is  
a fluorescent substance, said detecting is performed by  
15 a confocal microscope, and said analyzing is performed  
by a fluorescent correlation spectroscopy.

6. The method of detecting a polymorphism site  
according to claim 4, wherein the polymorphism site is  
a single nucleotide polymorphism.

20 7. A method of detecting a polymorphism site,  
comprising:

(1) hybridizing a test sample DNA fragment  
containing a sequence of a polymorphism site with a  
plurality of types of DNA probes respectively having  
25 sequences complementary to a plurality of sequences to  
be identified and contained in the test sample DNA  
fragment, and having a marker-substance labeled

nucleotide corresponding to the polymorphism sites,  
said plurality of types of probes being set so as to  
optically distinguish from each other; and

(2) reacting a nucleic acid synthetase having a  
5 repair function to a hybridized product obtained; and

(3) optically measuring and analyzing a change of  
the marker substance at a plurality of time points in  
the course of steps (1) and (2), thereby detecting the  
polymorphism site.

10 8. The method of detecting a polymorphism site  
according to claim 7, wherein said marker substance is  
a fluorescent substance, said detecting is performed by  
a confocal microscope, and said analyzing is performed  
by a fluorescent correlation spectroscopy.

15 9. The method of detecting a polymorphism site  
according to claim 7, wherein the polymorphism site is  
a single nucleotide polymorphism.

20 10. The method of detecting a polymorphism site  
according to claim 7, wherein said nucleic acid  
synthetase is an enzyme having an exonuclease activity.

11. A method of detecting a polymorphism site,  
comprising:

(1) preparing a test sample containing a  
polynucleotide;

25 (2) mixing a test sample with DNA probes  $PR_1$  to  
 $PR_n$  labeled with a detectable marker and capable of  
specifically binding to polymorphism sequences  $PS_1$  to

PS<sub>n</sub>, thereby binding the DNA probes PR<sub>1</sub> to PR<sub>n</sub> to the polynucleotide;

(3) detecting the DNA probes PR<sub>1</sub> to PR<sub>n</sub> present in a micro space; and

5 (4) analyzing detection results to determine, which one of the DNA probes PR<sub>1</sub> to PR<sub>n</sub> binds to the polynucleotide, thereby determining which one of the polymorphism sequences PS<sub>1</sub> to PS<sub>n</sub> corresponds to a nucleotide sequence of the polymorphism site.

10 12. The method of detecting a polymorphism site according to claim 11, wherein said marker substance is a fluorescent substance, said detecting is performed by a confocal microscope, and said analyzing is performed by a fluorescent correlation spectroscopy.

15 13. The method of detecting a polymorphism site according to claim 11, wherein said polynucleotide is a gene for a human histocompatible antigen.

14. A method of detecting a polymorphism site, comprising:

20 (1) placing a test sample and a plurality of antibodies respectively having a specificity to a plurality of antigens contained in the test sample and labeled with a fluorescent substance, in a same vessel, said fluorescent substance attached to each of said  
25 antibodies being set so as to be mutually distinguished; and

(2) optically measuring and analyzing

a positional change of the marker substance at a plurality of time points in the course of the reaction, thereby detecting the polymorphism site.

5 15. The method of detecting a polymorphism site according to claim 14, wherein said marker substance is a fluorescent substance, said detecting is performed by a confocal microscope, and said analyzing is performed by a fluorescent correlation spectroscopy.

10 16. The method of detecting a polymorphism site according to claim 14, wherein the polymorphism site is formed of a protein.

15 17. The method of detecting a polymorphism site according to claim 14, wherein the test sample is red blood cells and said antigen is a surface-layer antigen of red blood cells.

18. A method of detecting a polymorphism site, comprising:

20 (1) placing a test sample, a plurality of types of antigens respectively having a specificity to a plurality of antibodies to be identified contained in the test sample, and a plurality of antibodies which are the same type as said plurality of antibodies and which are labeled with a fluorescent substance, in a same vessel, the fluorescent substance labeled to each  
25 of the antibodies being set so as to distinguish from each other; and

(2) optically measuring and analyzing a

positional change of the marker substance at a plurality of time points in the course of the reaction, thereby detecting the polymorphism site.

19. The method of detecting a polymorphism site  
5 according to claim 18, wherein said marker substance is a fluorescent substance, said detecting is performed by a confocal microscope, and said analyzing is performed by a fluorescent correlation spectroscopy.

20. The method of detecting a polymorphism site  
10 according to claim 18, wherein the test sample is a body fluid derived from an organism.

21. The method according to any one of claims 1 to 3, wherein said optical determining includes measuring fluctuation of the marker substance.

22. The method according to any one of claims 4  
15 to 6, wherein said optical determining includes measuring fluctuation of the marker substance.

23. The method according to any one of claims 7  
20 to 10, wherein said optical determining includes measuring fluctuation of the marker substance.

24. The method according to any one of claims 11 to 13, wherein said optical determining includes measuring fluctuation of the marker substance.

25. The method according to any one of claims 14  
25 to 17, wherein said optical determining includes measuring fluctuation of the marker substance.

26. The method according to any one of claims 14

to 20, wherein said optical determining includes measuring fluctuation of the marker substance.

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